

## **REMARKS/ARGUMENTS**

### **Claim Amendments**

By the present amendment, claim 1 has been amended to remove the possibility that  $R^2$  is H and that  $R^3$  is " $-\text{CH}_2-\text{C}\equiv\text{C}-\text{R}^6$ ", along with the corresponding groups for  $R^6$  and to limit  $R^5$  to  $\text{C}_{1-6}$ alkyl. Claim 1 has been further amended to specify that the  $\text{H}_2$  pressure is between 30 bar and 80 bar. Basis for this latter amendment is found, for example, on page 23, line 26, for the upper limit of 80 bar, and in the Examples for the lower limit of 30 bar. Finally claim 1 has been amended to remove the second occurrence of the term "a base". The Applicant submits that the duplication of the term "a base" was a typographical error as supported, for example, by page 9, lines 18-21, of the application as filed.

Claims 8 to 11 have been amended to remove the possibility that  $R^2$  is H to be consistent with the amendment to claim 1.

Claim 16 has been amended to limit  $R^5$  to  $\text{C}_{1-4}$ alkyl to be consistent with the amendment to claim 1.

Claims 14 and 25-31 have been cancelled.

Claim 42 has been amended to replace " $\text{NHR}^6$ " with " $\text{NHR}^9$ ", to correct a clerical error.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been entered by the present amendment and entry of the amendments is respectfully requested. The Applicants reserve the right to file any of the cancelled subject matter in a divisional patent application.

The Office Action dated May 30, 2008 and the Advisory Action dated October 8, 2008 have been carefully considered. It is believed that the claims submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

#### **Recordation of Substance of Telephone Interview with Examiner Parsa**

In accordance with 37 CFR §1.113(b), the Applicants submit the following recordation of the substance of a telephone interview with the Examiner that occurred on October 30, 2008. The following information is to supplement the information provided on form PTOL-413 dated November 5, 2008, prepared by the Examiner.

Present at the interview were Examiner Parsa and Patricia Folkins (Agent for the Applicant). There were no exhibits shown or demonstrations conducted during the interview. The merits of all of the currently rejected claims were discussed. Specific prior art that was discussed was US 6,528,687 (Cobley).

The Agent for the Applicant identified that the main difference between the present application and the prior art is the identity of the group  $R^3$  on the imine. In Cobley,  $R^3$  is either aryl or benzyl or part of a cyclic structure. The Applicant noted that these types of imines are known in the art to have higher reactivity with respect to hydrogenation than the imines of the present application in which  $R^3$  is optionally substituted  $C_{1-2}$ alkyl and optionally substituted  $C_{3-10}$ cycloalkyl. The Applicant submits that a person skilled in the art would not have expected the hydrogenation method described in Cobley to work with the unactivated substrates that they are claiming.

Examiner Parsa suggested that comparative data would be helpful to show non-obviousness of the Applicant's method.

### 35 USC §103(a)

The Examiner has maintained a rejection of claims 1, 3, 5-19 and 25-53 under 35 USC §103(a) as being obvious in light of Cobley (U.S. Patent No. 6,528,687).

By the present amendment, the Applicant has amended claim 1 to remove the possibility that  $R^2$  is H and that  $R^3$  is " $-\text{CH}_2-\text{C}\equiv\text{C}-\text{R}^6$ ", along with the corresponding groups for  $R^6$ , and to limit  $R^5$  to  $\text{C}_{1-6}$ alkyl. Claim 1 has been further amended to specify that the  $\text{H}_2$  pressure is between 30 bar and 80 bar. For the reasons that follow, the Applicant submits that Cobley does not render obvious the claims of the present application.

The Applicant submits that Cobley described and claims a process for hydrogenation that is applicable only to activated imines, i.e. imines in which the nitrogen of the imine is substituted with various activating groups, such as aryl or benzyl moieties or is part of a cyclic structure. To the contrary, the process of the present application is useful for the hydrogenation of unactivated imines, wherein the substituent on the nitrogen imine is selected from optionally substituted  $\text{C}_1$  to  $\text{C}_2$  alkyl and  $\text{C}_{3-10}$ cycloalkyl and  $R^2$  is other than H.

In the Advisory Action dated November 5, 2008, the Examiner states that by allowing  $R^3$  to be optionally substituted in the claims of the present application, this reads on Cobley. The Applicant respectfully disagrees and notes that the optional substituents that are allowed on  $R^3$  in the present claims are halo,  $\text{NO}_2$ ,  $\text{OC}_{1-6}$ alkyl,  $\text{N}(\text{C}_{1-6}\text{alkyl})_2$  and  $\text{C}_{1-6}$ alkyl. None of these groups contribute to the activation of the imine towards hydrogenation and none of these groups make  $R^3$  read on Cobley.

To further distinguish the hydrogenation method claimed in the present application, and that of Cobley, the Applicant has amended claim 1, and accordingly all remaining claims dependent thereon to specify that the hydrogenation is carried out at a hydrogen

pressure between 30 bar and 80 bar. In Cobley, all of the reactions were performed using a hydrogen pressure of less than 30 bar.

In support of the fact that the imines of the present application are far less reactive than those described and claimed in Cobley, the Applicant has submitted herewith a Declaration under 37 CFR §1.132 providing side-by-side reaction results comparing the reactivity of the imines described in Cobley with those of the present application. As illustrated in the Declaration, the Applicant has provided evidence that the process as described in Cobley is not able to effectively hydrogenate the imines covered by claim 1 of the present application. The Applicant has demonstrated that activated imines (such as phenyl and benzyl substituted imines) are converted to their corresponding amines in high yields, as expected, using the processes as described in Cobley. However, unactivated imines (such as a cyclopentyl-substituted imine) are converted to their corresponding amines in very low yields, using the processes as disclosed in Cobley.

The Applicant submits that the low conversions of unactivated imines is in contrast to the very high conversions obtained using the process of the present application. The Applicant directs the Examiner's attention to Example 1.7 of the present application, wherein a cyclopentyl-substituted imine is converted to its corresponding amine using various catalysts, with yields of up to 97% with a hydrogen pressure of 50 bar. The Applicant notes that this is the same imine that was converted to the corresponding amine in only very low yields using the processes described in Cobley, as seen in the attached Declaration.

Accordingly, the Applicant respectfully submits that a person skilled in the art at the time the present application was made would not have realized from the teachings in Cobley that the unactivated imines of the present application could be hydrogenated using a catalytic system comprising a base and a ruthenium complex comprising a diamine and a diphosphine ligand or a monodentate phosphine ligand. Cobley purposely limits the substrates for his claimed method to activated imines, highlighting

that, at the time the present application was filed, the general knowledge was that the unactivated imines of the present application could not be hydrogenated using this method. Surprisingly, the present Applicant was able to hydrogenate these unactivated imines in excellent yields and reasonable amounts of time. This is completely unexpected and non-obvious in view of the teachings of Cobley.

It should be noted that claims 14 and 25-31 have been cancelled herein, rendering the Examiner's rejection of these claims moot.

In light of the above, the Applicant requests that the Examiner's rejection of claims 1, 3, 5-19 and 25-53 under 35 USC §103(a) as being obvious in light of Cobley be withdrawn.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, he is invited to contact the undersigned by telephone at (416) 957-1665 at his convenience.

Respectfully submitted,  
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